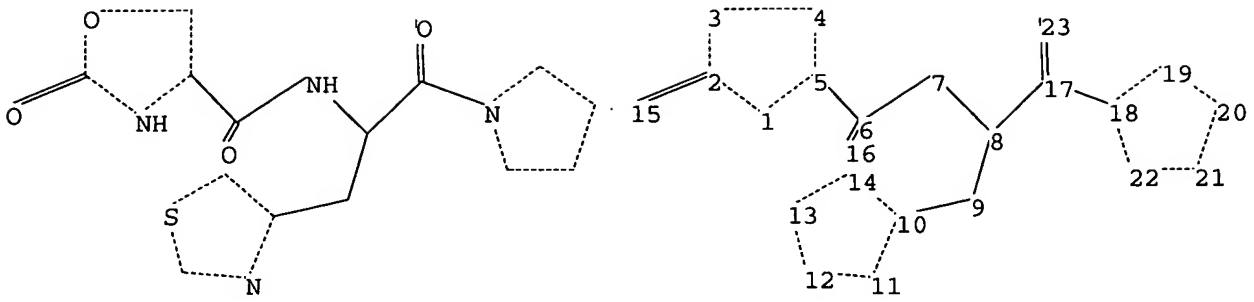
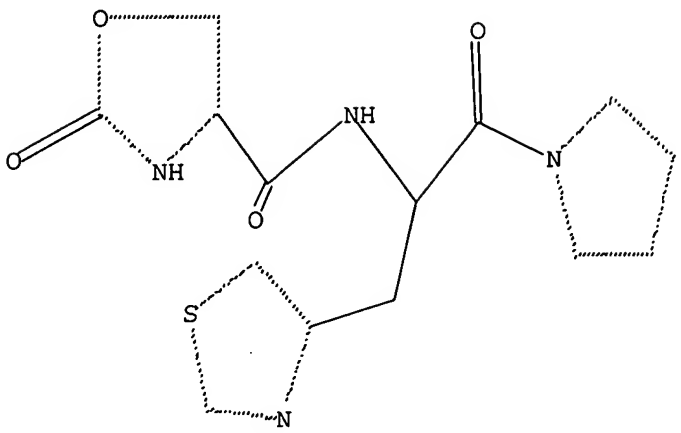


chain nodes :
6 7 8 9 15 16 17 23
ring nodes :
1 2 3 4 5 10 11 12 13 14 18 19 20 21 22
chain bonds :
2-15 5-6 6-7 6-16 7-8 8-9 8-17 9-10 17-18 17-23
ring bonds :
1-2 1-5 2-3 3-4 4-5 10-11 10-14 11-12 12-13 13-14 18-19 18-22 19-20
20-21 21-22
exact/norm bonds :
1-2 1-5 2-3 2-15 3-4 4-5 6-7 6-16 7-8 10-11 10-14 11-12 12-13 13-14
17-18 17-23 18-19 18-22 19-20 20-21 21-22
exact bonds :
5-6 8-9 8-17 9-10
isolated ring systems :
containing 1 : 10 : 18 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 11:01:08 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        3 TO ITERATE

100.0% PROCESSED         3 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               1 TO       80

L2             1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 11:01:15 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       71 TO ITERATE

100.0% PROCESSED        71 ITERATIONS                                27 ANSWERS
SEARCH TIME: 00.00.01

L3            27 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   166.94     167.15

FILE 'CAPLUS' ENTERED AT 11:01:21 ON 24 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 24 Jun 2006 VOL 145 ISS 1
FILE LAST UPDATED: 23 Jun 2006 (20060623/ED)

=> s l3
L4 6 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:234805 CAPLUS
DOCUMENT NUMBER: 144:299445
TITLE: A pharmaceutical composition for treating ataxia, multiple system atrophy or balance disorders
INVENTOR(S): Yoshikawa, Takayoshi; Katsuura, Goro
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006028277	A1	20060316	WO 2005-JP16994	20050908

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-261977 A 20040909
US 2004-613717P P 20040929

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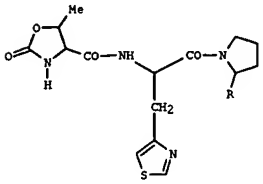
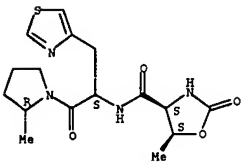


I

AB This invention provides a pharmaceutical composition for treating spinocerebellar ataxia (or atrophy, degeneration) or multiple system atrophy, or for improving ataxia or equilibrium disturbance comprising a compound

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(compn. contg. oxooxazolidinylcarbonyl thiazolylalanyl pyrrolidine deriv. for treating ataxia, multiple system atrophy or balance disorders)
RN 879122-88-0 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, monohydrate, (4S,5S)- (9CI) (CA INDEX NAME)

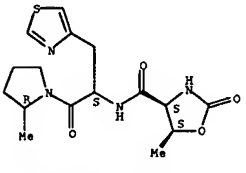
Absolute stereochemistry.



● H_2O

IT **204386-76-5P 879122-87-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(composition containing oxooxazolidinylcarbonyl thiazolylalanyl pyrrolidine
derivative for treating ataxia, multiple system atrophy or balance disorders)
RN 204386-76-5 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

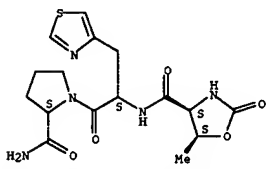
Absolute stereochemistry. Rotation (-).



RN 879122-87-9 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, trihydrate, (4S,5S)- (9CI) (CA INDEX NAME)

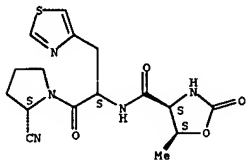
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
of the formula I (R = Me, cyano, carbamoyl), a pharmaceutically acceptable salt, or a solvate thereof as an active ingredient. For example, I trihydrate (R = Me) was prepd. (yield 80.3%) and its effect on ataxia of Rolling Mouse Nagoya was investigated. An improvement of ataxia of oral I trihydrate (R = Me) at 1 mg/kg and 3 mg/kg was demonstrated, being ≥ 30 and ≥ 100 times more effective than control compds., resp. A capsule formulation contg. compd. I 10 mg, lactose 90 mg, corn starch 42 mg, and hydroxypropyl cellulose 3 mg was provided.
IT **204385-91-1 204386-74-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition containing oxooxazolidinylcarbonyl thiazolylalanyl pyrrolidine
derivative for treating ataxia, multiple system atrophy or balance disorders)
RN 204385-91-1 CAPLUS
CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



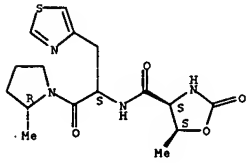
RN 204386-74-3 CAPLUS
CN 4-Oxazolidinecarboxamide, N-[(1S)-2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **879122-88-0**
RL: RCT (Reactant); RACT (Reactant or reagent)

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



●3 H_2O

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:171718 CAPLUS
DOCUMENT NUMBER: 136:232293
TITLE: Preparation process of chiral N-(2-(4-thiazolyl)-1-(2-methylpyrrolidinylcarbonyl)ethyl)-4-methyl-2-oxo-oxazolidine-5-carbamide as antiparkinsonian agent
INVENTOR(S): Shinohara, Shunji; Koike, Katsumi
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017954	A1	20020307	WO 2001-JP7410	20010829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001082527	A5	20020313	AU 2001-82527	20010829
CA 2420537	AA	20030225	CA 2001-2420537	20010829
EP 1321151	A1	20030625	EP 2001-961157	20010829
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003191120	A1	20031009	US 2003-362922	20030227

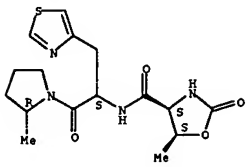
PRIORITY APPLN. INFO.: JP 2000-262618 A 20000831
WO 2001-JP7410 W 20010829
OTHER SOURCE(S): CASREACT 136:232293; MARPAT 136:232293
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; A = thiazolyl, imidazolyl; X = single bond, O, S; Y = alkyl, CONR1R2; Z = Q; m = 0, 1, 2, 3, 4; R1, R2 independently = H, alkyl; R3 = H, alkyl; R4 = H, alkyl; R5 = alkyl, H; W = (CH2)n; n = 0, 1, 2, 3] prodrugs, pharmaceutically acceptable salts, solvates, and prodrugs of title compds. are prepared and are found to be useful as therapeutic or preventive agents for Parkinson disease. Thus, the title compound II was prepared from N-tert-butoxycarbonyl-L-(4-thiazolyl)alanine, diphenyldiazomehane, and (4S-cis)-5-methyl-2-oxo-4-oxazolidinecarboxylic acid in five steps.
IT **204386-76-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(prepn. process of chiral N-(2-(4-thiazolyl)-1-(2-methylpyrrolidinylcarbonyl)ethyl)-4-methyl-2-oxo-oxazolidine-5-carbamide as antiparkinsonian agent)
RN 204386-76-5 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

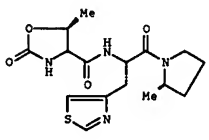


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:51292 CAPLUS
DOCUMENT NUMBER: 136:123639
TITLE: Enteric compositions containing physiologically active peptides
INVENTOR(S): Sugita, Katsuji; Yoshikawa, Takayoshi
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004016	A1	20020117	WO 2001-JP5543	20010628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001066347	A5	20020121	AU 2001-66347	20010628
EP 1300155	A1	20030409	EP 2001-943852	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003175350	A1	20030918	US 2003-332490	20030109

PRIORITY APPLN. INFO.: JP 2000-209923 A 20000711
WO 2001-JP5543 W 20010628
OTHER SOURCE(S): MARPAT 136:123639
GI

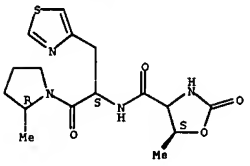


I

AB Disclosed are enteric compns. for oral administration excellent in absorbability, containing TSH-releasing hormone (TRH) or derivs. thereof as the medicinally active ingredient. A coated enteric tablet was prepared from a TRH derivative I 30, corn starch 17.4, hydroxypropyl cellulose SL 0.7, partially alphatized starch 1.4, magnesium stearate 0.5, hydroxypropyl Me cellulose (HPMC2910E) 0.8, hydroxypropyl Me cellulose acetate succinate (HPMCAS-LF) 6, tri-Et citrate 0.7, and talc 1.3 mg.
IT **389119-11-3**

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric compns. contg. TRH derivs. and enteric materials)
RN 389119-11-3 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



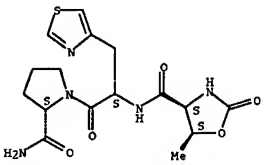
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:690970 CAPLUS
DOCUMENT NUMBER: 131:314180
TITLE: Oral preparations containing TRH derivatives
INVENTOR(S): Sugita, Katsuji; Satoh, Norihito; Yoshikawa, Takanori
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953941	A1	19991028	WO 1999-JP2006	19990415
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: JP 1998-104993 A 19980415
AB Prepns. for the oral administration of TRH derivs. characterized by containing the TRH derivs., medium-chain triglycerides and, if desired, lecithin. Use of these prepns. makes it possible to improve the oral absorbability of the TRH derivs. thereby elevating the bioavailability thereof.
IT **204385-91-1 204386-74-3 204386-76-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (oral prepns. containing TRH derivs.)
RN 204385-91-1 CAPLUS
CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

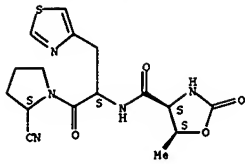
Absolute stereochemistry. Rotation (-).



RN 204386-74-3 CAPLUS
CN 4-Oxazolidinecarboxamide, N-[(1S)-2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

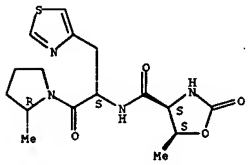
Absolute stereochemistry. Rotation (-).

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 204386-76-5 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:576919 CAPLUS
DOCUMENT NUMBER: 131:200096
TITLE: Process for producing 4-thiazolylmethyl halide, β-(4-thiazolyl)alanine, and peptide
INVENTOR(S): Uenaka, Masasaki; Nagai, Masahiko; Kobayashi, Naotake
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945000	A1	19990910	WO 1999-JP975	19990301
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926423	A1	19990920	AU 1999-26423	19990301
EP 1069118	A1	20010117	EP 1999-906538	19990301
EP 1069118	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TW 530052	B	20030501	TW 1999-88103061	19990301
AT 277024	E	20041015	AT 1999-906538	19990301
ES 2229680	T3	20050416	ES 1999-906538	19990301
US 6506903	B1	20030114	US 2000-622441	20000817

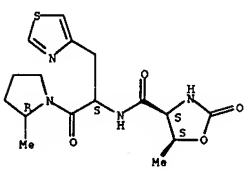
PRIORITY APPLN. INFO.: JP 1998-49259 A 19980302
WO 1999-JP975 W 19990301
OTHER SOURCE(S): CASREACT 131:200096; MARPAT 131:200096
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The process for producing a compound represented by general formula (I) (wherein R1 is hydrogen or halogeno and X is halogeno) comprises reacting 4-methylthiazole with an N-halosuccinimide in a solvent in the presence of a radical initiator. A process for producing a 4-thiazolylalanine derivative (II and III; R2' is an amino acid-protecting group) comprises coupling of 4-thiazolylmethyl halide (I) with aminomalonate of formula R2NHCH(CO2R3)2 (R2 is an amino acid protective-group; R3 is lower alkyl) to give amino(4-thiazolylmethyl)malonate [I; X = C(CO2R3)2NHR2], followed by hydrolysis, decarboxylation, and optical resolution. Moreover, the 4-thiazolylalanine derivative undergoes peptide bond formation to give dipeptide amides [IV; Y is (un)substituted alkyl]. Thus, 163.5 g 4-methylthiazole was dissolved in 3 L chlorobenzene, heated to 130°, treated with 242 g N-chlorosuccinimide and 13.5 g 2,2'-azobisbutyronitrile, and kept at 160° for 15 min to give, after workup and treatment with 4 N HCl/EtOAc, 43.5% 4-

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
chloromethylthiazole hydrochloride (V.HCl). V.HCl (154 g) was dissolved in 0.5 L H2O and treated with 3 L toluene and 113 g NaHCO3, followed by washing the org. layer and extg. the aq. layer, drying the combined org. layer over MgSO4, and distg. off the solvent, to give 98% V. To 20% NaOMe/MeOH (306 g) was added 96 g di-Et acetamidomalonate, refluxed for 2 h, treated with a soln. of 124 g V contg. 10% PhMe in ethanol (0.6 L) at 50°, and stirred at 50° for 3 h to give 72.5% I [X = C(CO2Et)2NHAc]. The latter diester (201.2 g) was dissolved in 3 N aq. NaOH (960 mL), stirred at 50° for 1.5 h, treated with 100 ML concd. HCl to adjust pH = 3.5, stirred at 100° for 3 h, cooled, treated with 120 g immobilized acylase, followed by adjusting pH = 6.7, stirred at 37° for 4 h, and filtered. To the filtrate were added 500 mL dioxane, 90.8 g di-tert-Bu dicarbonate, and 58 mL Et3N, stirred at 25° for 2 h, and extd. with 1 L EtOAc to give 40% III (R2' = Boc). The latter N-tert-butoxycarbonyl-(4-thiazolyl)alanine was converted into a dipeptide (VI) in 4 steps.
IT **204386-76-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolylmethyl halide by halogenation of methylthiazole, its coupling with aminomalonate to amino(thiazolylmethyl)malonate, and conversion to β-(4-thiazolyl)alanine and peptide)
RN 204386-76-5 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:163612 CAPLUS
DOCUMENT NUMBER: 128:230695
TITLE: Preparation of novel peptide derivatives having thiazolyl-alanine residue
INVENTOR(S): Sugawara, Tamio; Yoshikawa, Takayoshi; Tada, Yukio
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

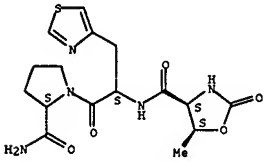
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808867	A1	19980305	WO 1997-JP2917	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2264268	AA	19980305	CA 1997-2264268	19970822
CA 2264268	C	20031111		
AU 9738680	A1	19980319	AU 1997-38680	19970822
AU 713133	B2	19991125		
EP 933379	A1	19990804	EP 1997-935856	19970822
EP 933379	B1	20060322		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9712081	A	19990824	BR 1997-12081	19970822
CN 1235610	A	19991117	CN 1997-199248	19970822
JP 3234236	B2	20011204	JP 1998-511459	19970822
AT 321067	E	20060415	AT 1997-935856	19970822
TW 492977	B	20020701	TW 1997-86112314	19970827
MX 9901831	A	20000331	MX 1999-1831	19990224
KR 2000035930	A	20000626	KR 1999-701667	19990227
US 6319902	B1	20011120	US 1999-230821	19990512
PRIORITY APPLN. INFO.:			JP 1996-226386 A	19960828
			JP 1997-90529 A	19970409
			WO 1997-JP2917 W	19970822
OTHER SOURCE(S):	MARPAT 128:230695			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

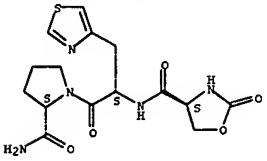
AB Peptide derivs. represented by general formula [I; A = 4- or 5-thiazolyl; Y = single bond, O, S; m = 0-4; Y = (un)substituted alkyl or CO2H, cyano, CONR1R2; wherein R1, R2 = H or (un)substituted alkyl or NR1R2 = (un)substituted nonarom. heterocyclyl optionally containing O, N, or S; Z = Q,

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



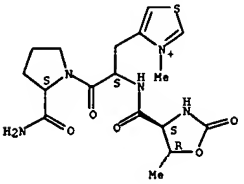
RN 204385-98-8 CAPLUS
CN L-Prolinamide, (4S)-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 204386-25-4 CAPLUS
CN L-Prolinamide, (4S,5R)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(3-methylthiazolium-4-yl)-L-alanyl-, iodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● I-

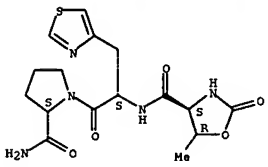
RN 204386-28-7 CAPLUS

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Q1; R3 = H, (un)substituted alkyl, CO2H, or acyl; R4, R5 = H, (un)substituted alkyl; W = (CH2)n, O, S, (un)substituted NH; wherein n = 0, 1, 2, or 3] or pharmacol. acceptable salts or hydrates thereof are prepd. These peptide compds. have improved central nerve activating effects such as sustained acetylcholine-releasing effect, antireserpine effect and spontaneous motility increasing effect as compared with the publicly known TSH releasing hormone TSH-releasing hormone (TRH) (H-pGlu-His-Pro-NH2) and TRH derivs. Thus, L-pyroglutamic acid was condensed with 3-(4-thiazolyl)-L-alanyl-L-prolinamide hydrochloride using DCC and N-hydroxysuccinimide in DMF to give the title compd. (II; R = Q2). II (R = Q3) at 24 μmol/kg p.o. increased ≤260% release of acetylcholine from brain in rat 350 h after administration of the compd.

IT 204385-84-2P 204385-91-1P 204385-98-8P
204386-25-4P 204386-28-7P 204386-30-1P
204386-35-6P 204386-37-8P 204386-39-0P
204386-41-4P 204386-66-3P 204386-67-4P
204386-68-5P 204386-70-9P 204386-71-0P
204386-72-1P 204386-73-2P 204386-74-3P
204386-75-4P 204386-76-5P 204386-77-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel peptide derivs. having thiazolylalanine residue as central nerve activators)

RN 204385-84-2 CAPLUS
CN L-Prolinamide, (4S,5R)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

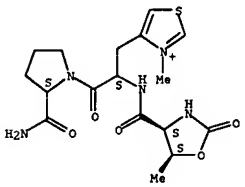


RN 204385-91-1 CAPLUS
CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(3-methylthiazolium-4-yl)-L-alanyl-, iodide (9CI) (CA INDEX NAME)

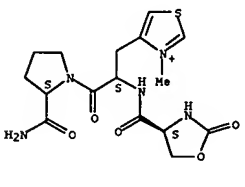
Absolute stereochemistry. Rotation (-).



● I-

RN 204386-30-1 CAPLUS
CN L-Prolinamide, (4S)-2-oxo-4-oxazolidinecarbonyl-3-(3-methylthiazolium-4-yl)-L-alanyl-, iodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

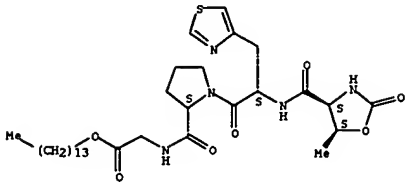


● I-

RN 204386-35-6 CAPLUS
CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl-, tetradecyl ester (9CI) (CA INDEX NAME)

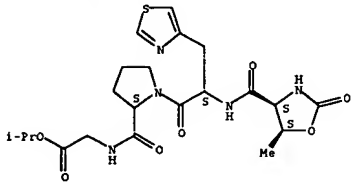
Absolute stereochemistry. Rotation (-).

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 204386-37-8 CAPLUS
CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)

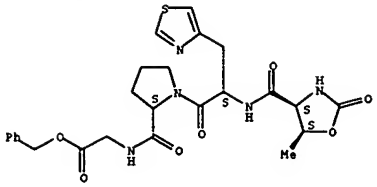
Absolute stereochemistry. Rotation (-).



RN 204386-39-0 CAPLUS
CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

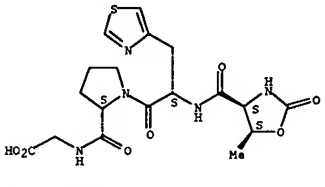
Absolute stereochemistry. Rotation (-).

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



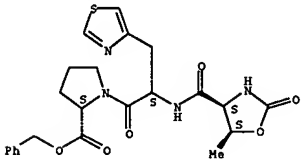
RN 204386-41-4 CAPLUS
CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 204386-66-3 CAPLUS
CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

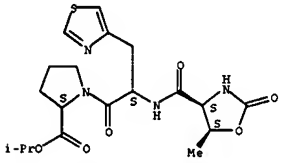
Absolute stereochemistry. Rotation (-).



L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

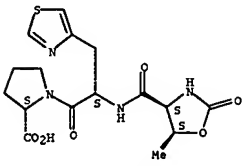
RN 204386-67-4 CAPLUS
CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



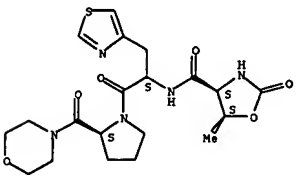
RN 204386-68-5 CAPLUS
CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 204386-70-9 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[2-[2-(4-morpholinylcarbonyl)-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, [4S-[4α[R*(R*)],5α]]- (9CI) (CA INDEX NAME)

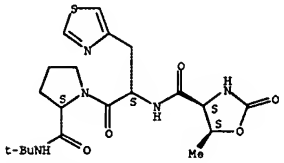
Absolute stereochemistry. Rotation (-).



L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

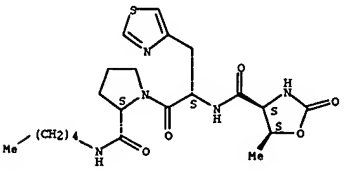
RN 204386-71-0 CAPLUS
CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 204386-72-1 CAPLUS
CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-N-pentyl- (9CI) (CA INDEX NAME)

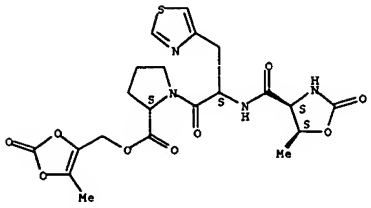
Absolute stereochemistry. Rotation (-).



RN 204386-73-2 CAPLUS
CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl ester (9CI) (CA INDEX NAME)

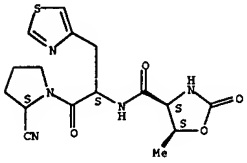
Absolute stereochemistry. Rotation (-).

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



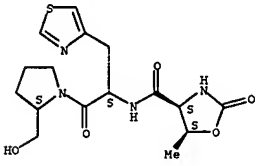
RN 204386-74-3 CAPLUS
CN 4-Oxazolidinecarboxamide, N-[(1S)-2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 204386-75-4 CAPLUS
CN 4-Oxazolidinecarboxamide, N-[2-[2-(hydroxymethyl)-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, [4S-[4α[R*(R*)],5α]]- (9CI) (CA INDEX NAME)

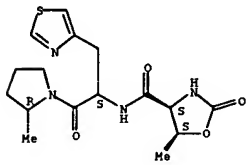
Absolute stereochemistry. Rotation (-).



L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

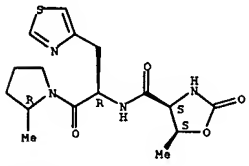
RN 204386-76-5 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 204386-77-6 CAPLUS
CN 4-Oxazolidinecarboxamide, 5-methyl-N-[2-(2-methyl-1-pyrrolidinyl)-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, [4S-[4α[S*(S*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT